HPV Testing in Head and Neck Squamous Cell Carcinomas (HNSCC)

Bedard Symposium 2017
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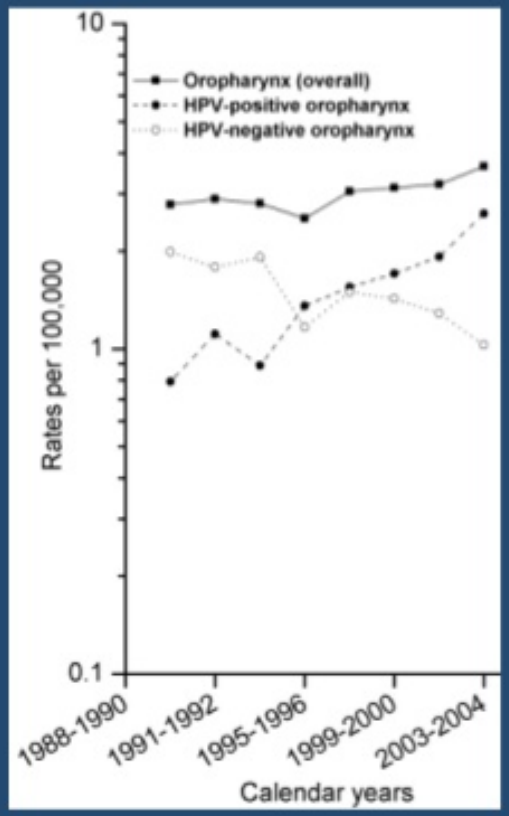
The HPV-HNSCC Epidemic

Rapidly Changing Incidence of HPV-Positive vs HPV-Negative HNC

In US from 1988 to 2004:

- ↘ Oropharynx rates increasing overall
- ↘ HPV-positive increased by 225%
- ↘ HPV-negative declined by 50%

Similar changes in numerous developed countries worldwide



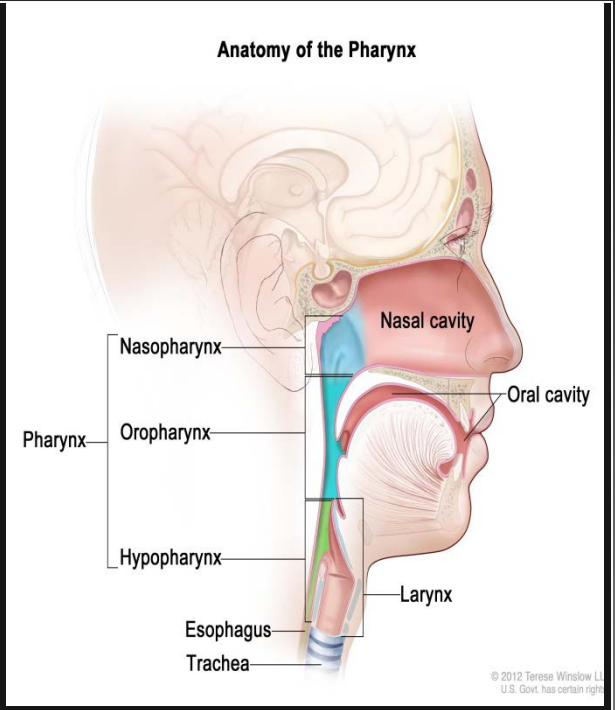
Chaturvedi et al, 2011; Chaturvedi et al, 2013.

Clinical Presentation of HPV-Related HNSCC is Different From Smoking Related Cancer

- Young, educated males
- Changing sexual practices- increased number of oral sex partners in young men
- Lack a significant history of tobacco or alcohol abuse

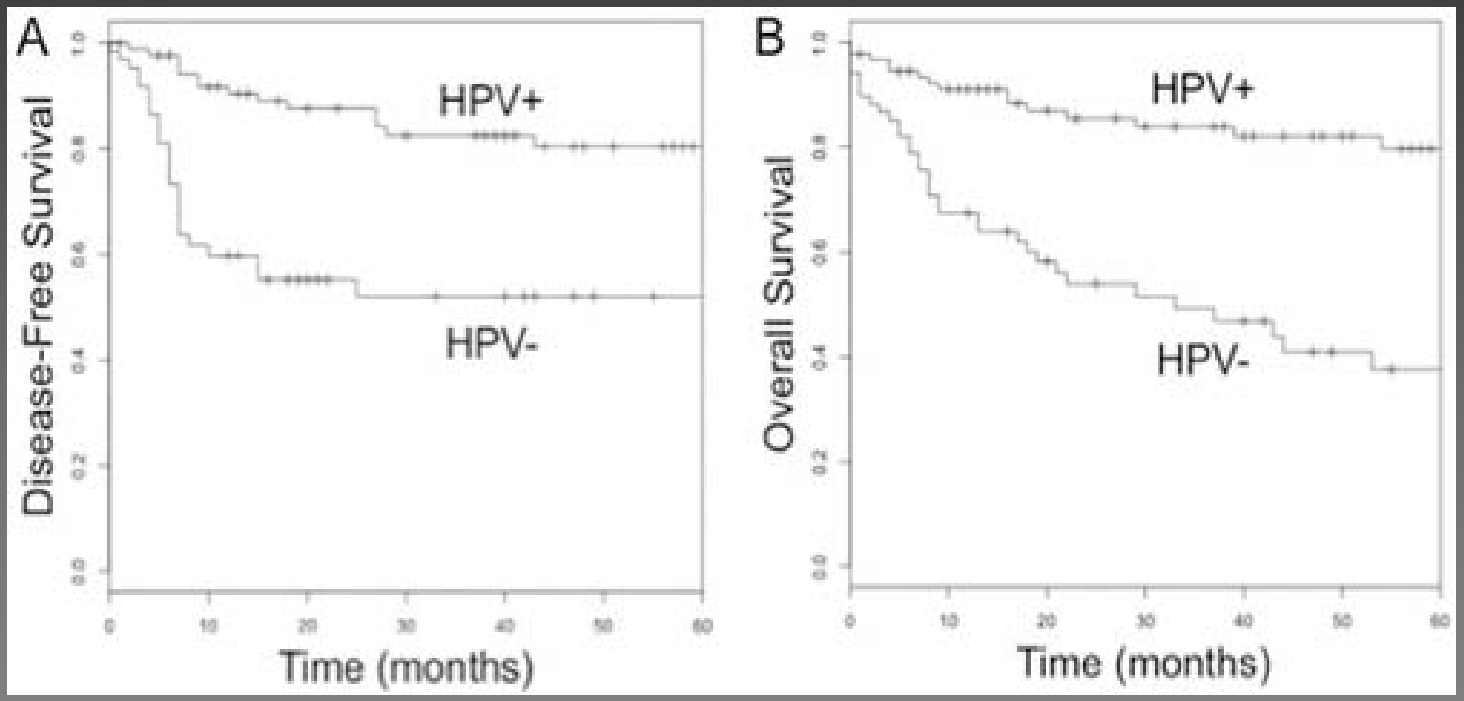
HR-HPV at Various Sites

- Oropharynx: 80-90%
- Sinonasal cavity: 20-25%
- Oral cavity: 3-6%
- Nasopharynx:7%
- Larynx:<5%
- Others

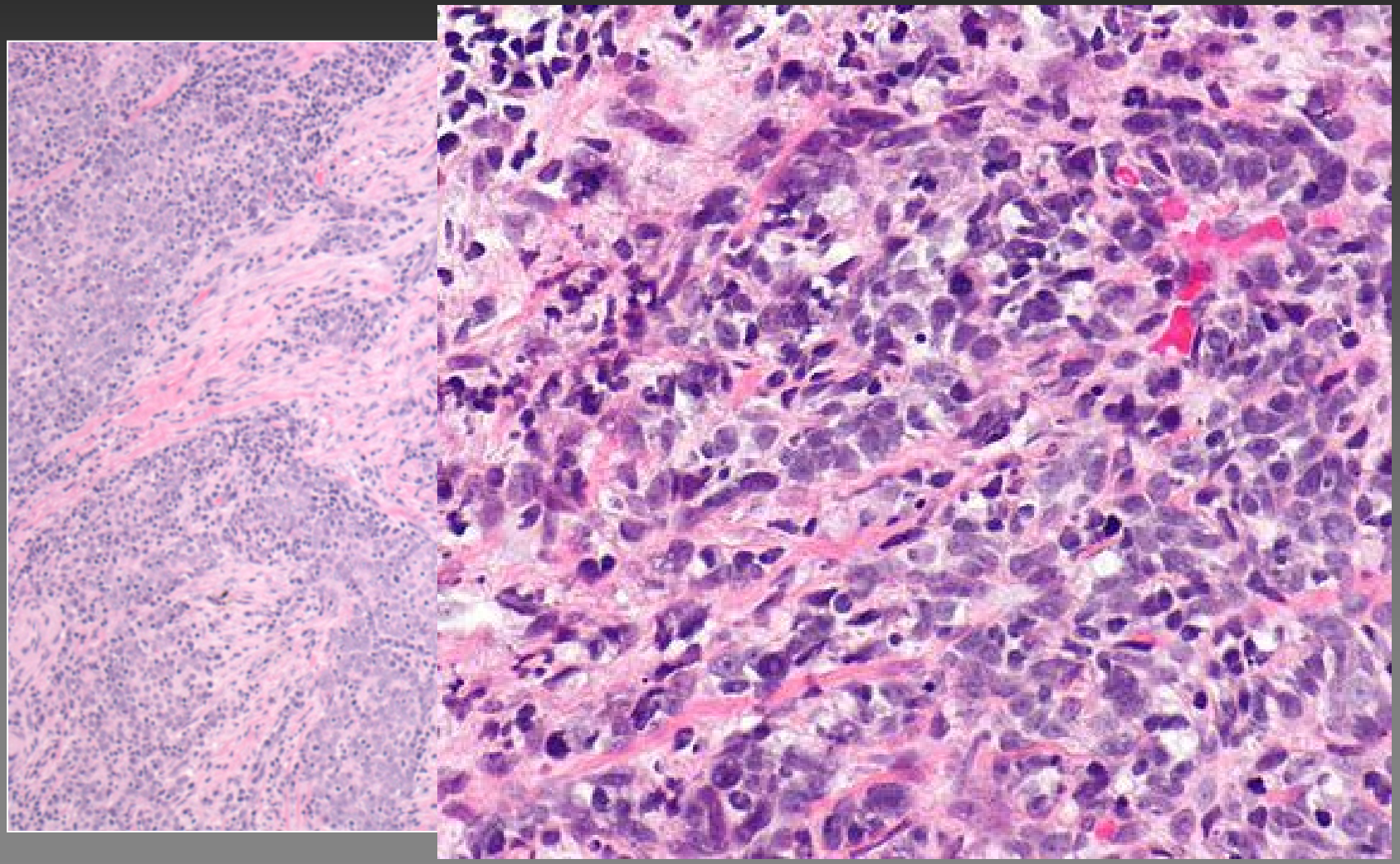


HPV-positive oropharyngeal SCC have a better prognosis than HPV-negative cancers

Prognosis is Better for HPV-Positive Tumours



HPV-positive Oropharyngeal SCC

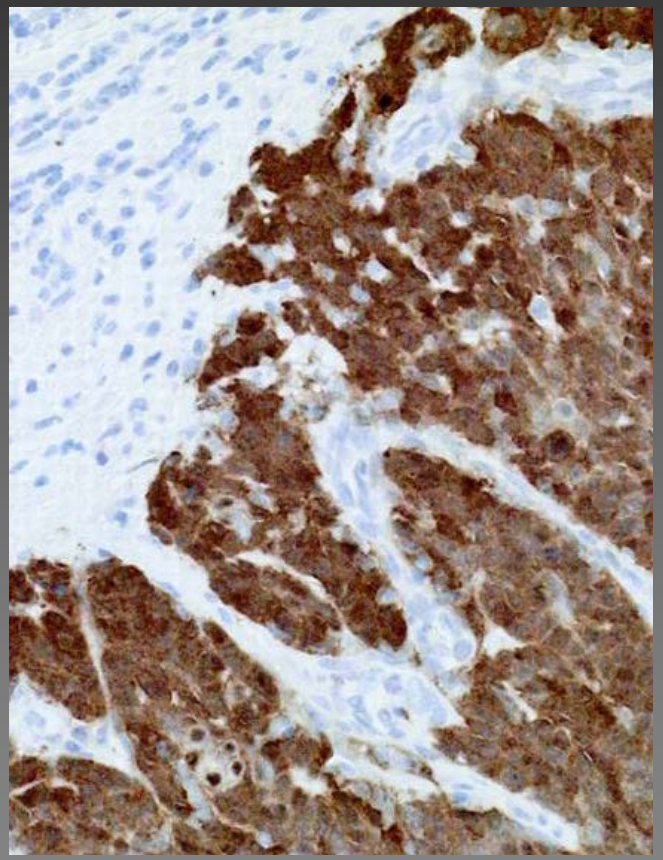


CCO Guidelines for HPV Testing in Head and Neck SCC

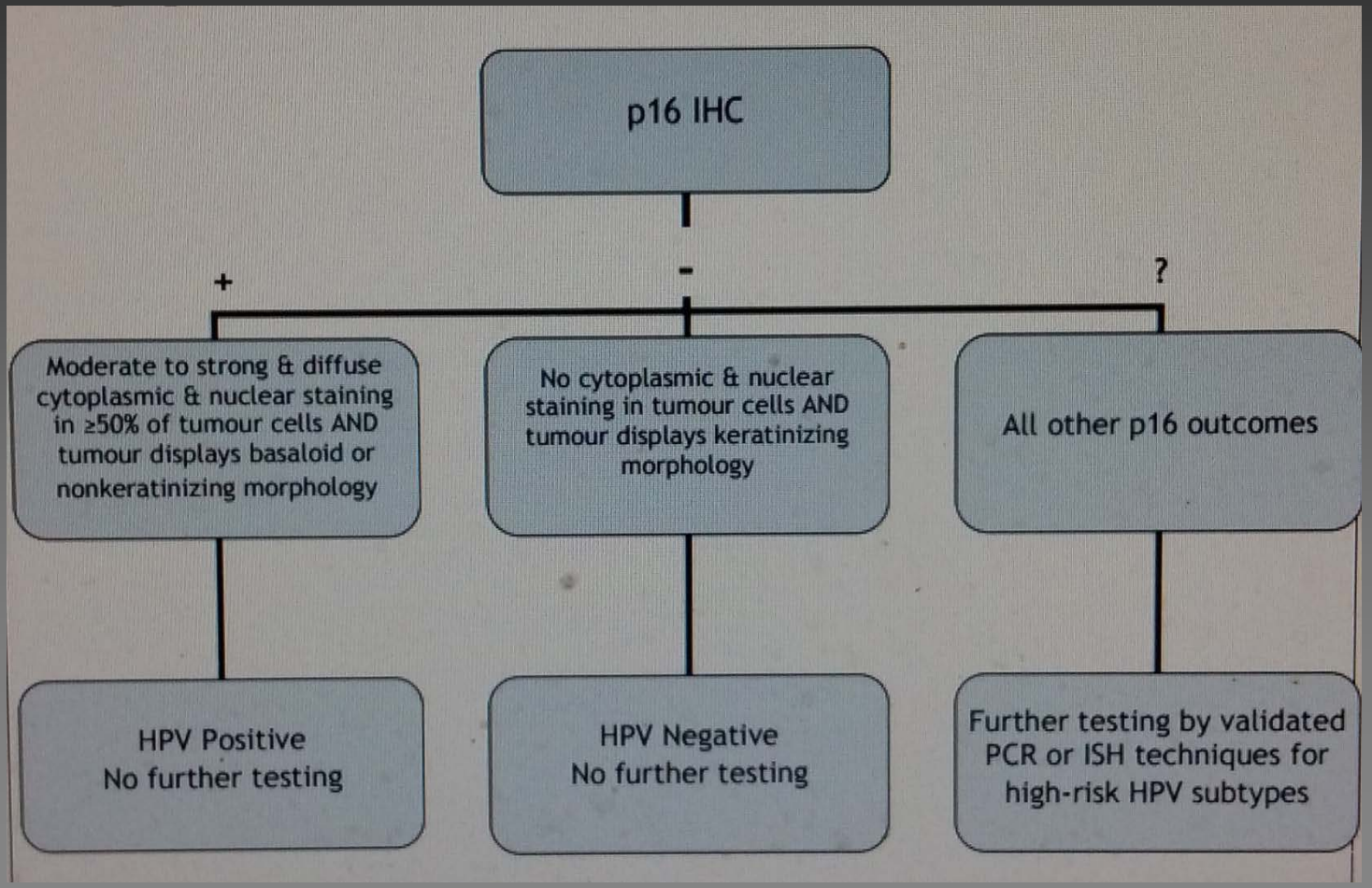
- Tumours of all patients presenting with oropharyngeal SCC should be routinely tested for HPV status
- Neck nodal tissue of patients with metastatic squamous cell carcinoma from an unknown head and neck primary should be routinely tested for HPV
- HPV status in oropharyngeal SCC be initially determined using IHC staining for p16

Staining for p16 Can Be Considered Positive When the Following Criteria are Met:

- Cytoplasmic and nuclear staining
- Staining is moderate to strong and diffuse
- Staining is present in at least 70% of tumour cells



p16 as a Surrogate Marker for HPV



Methods for Determining HR-HPV Status in HNSCC

• IHC for p16	High sensitivity, reduced specificity, esp. outside OP
• PCR for HPV DNA	High sensitivity, but low specificity
• *ISH* for HPV DNA	High specificity; reduced sensitivity at low viral load
• RT-PCR E6/E7 mRNA	Needs fresh frozen tissue
• *ISH* for HPV RNA	Reduced sensitivity at low viral load
• IHC for E6/E7	Low sensitivity, poor performance
• Cytology Test Platforms	Validation studies needed

CAP

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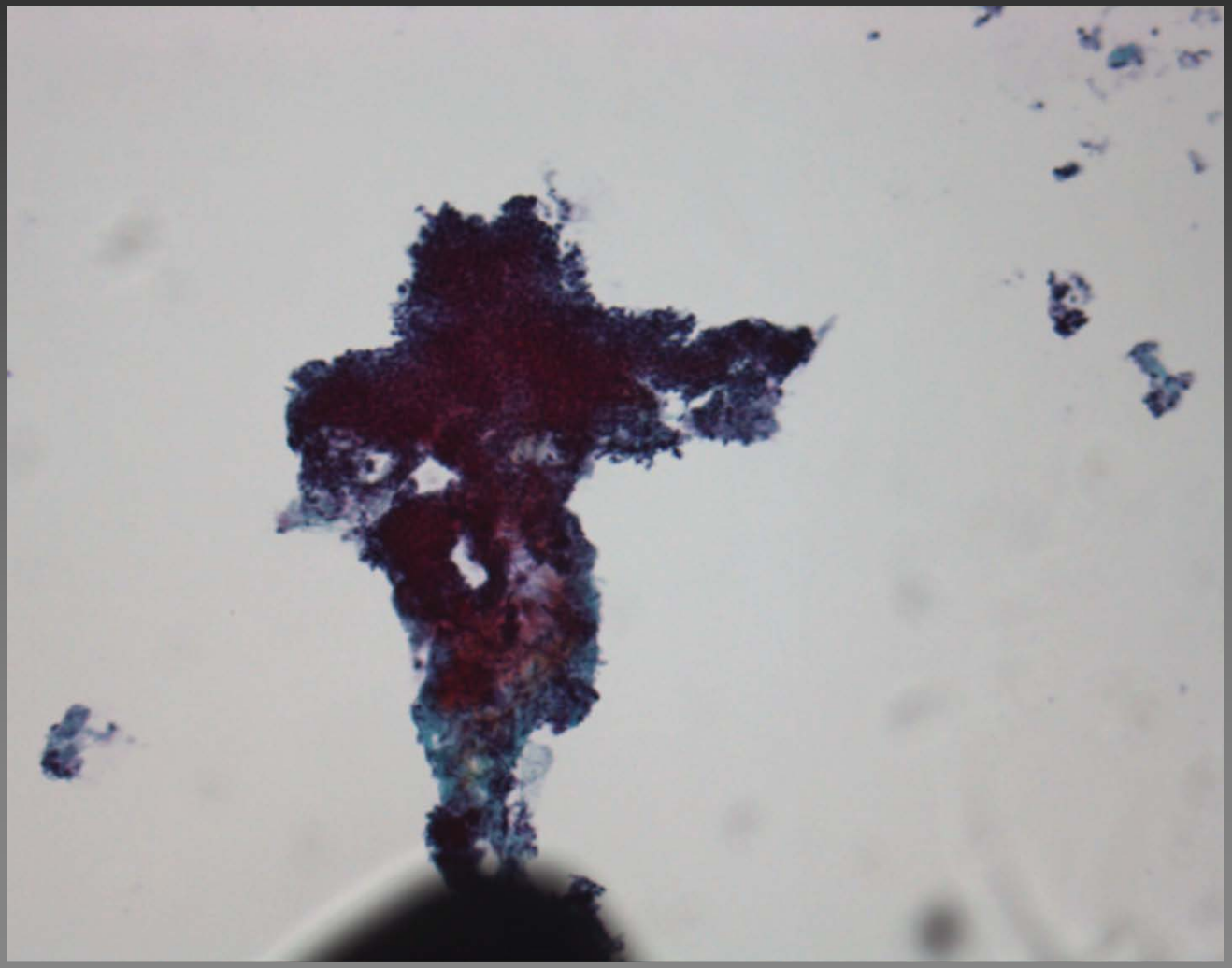
HPV Associated SCC – Presentation as a Neck Mass

- Initial presentation as a neck mass with unknown primary is not uncommon
- Often cystic
- Cytology has an important role:
  - Diagnosis
  - Determination of HPV status – directs search for primary tumour

Case #1: FNA of Neck Mass



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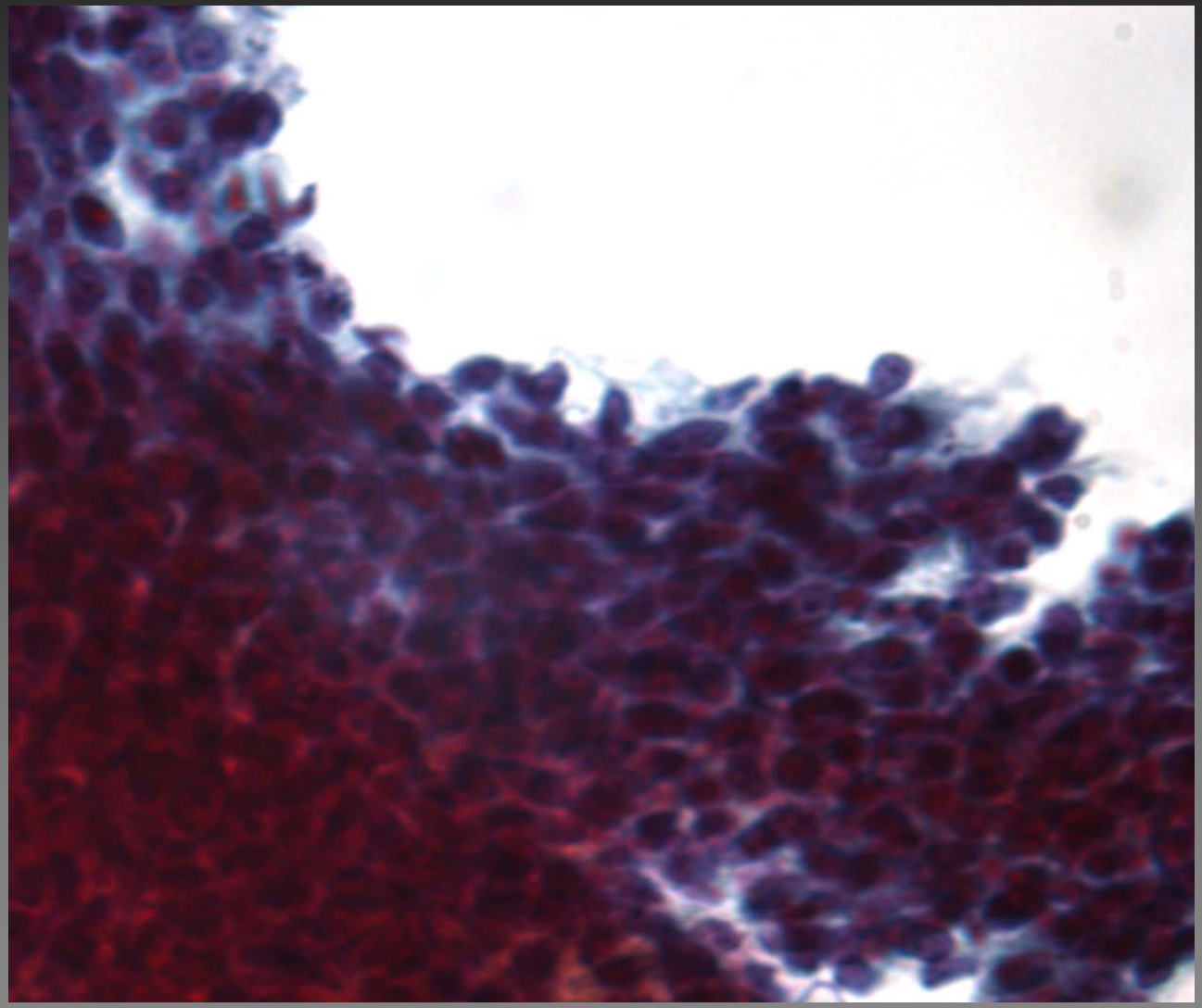
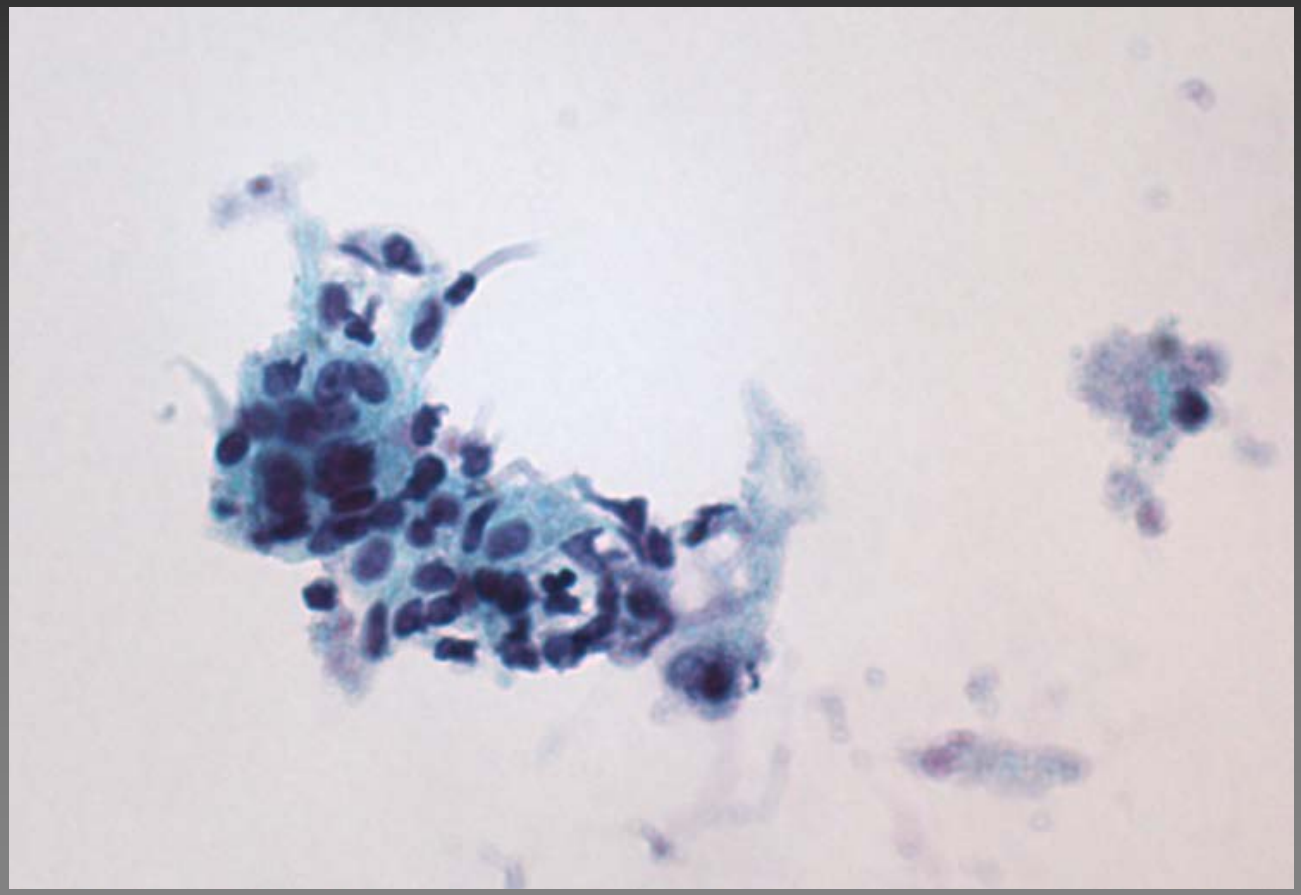
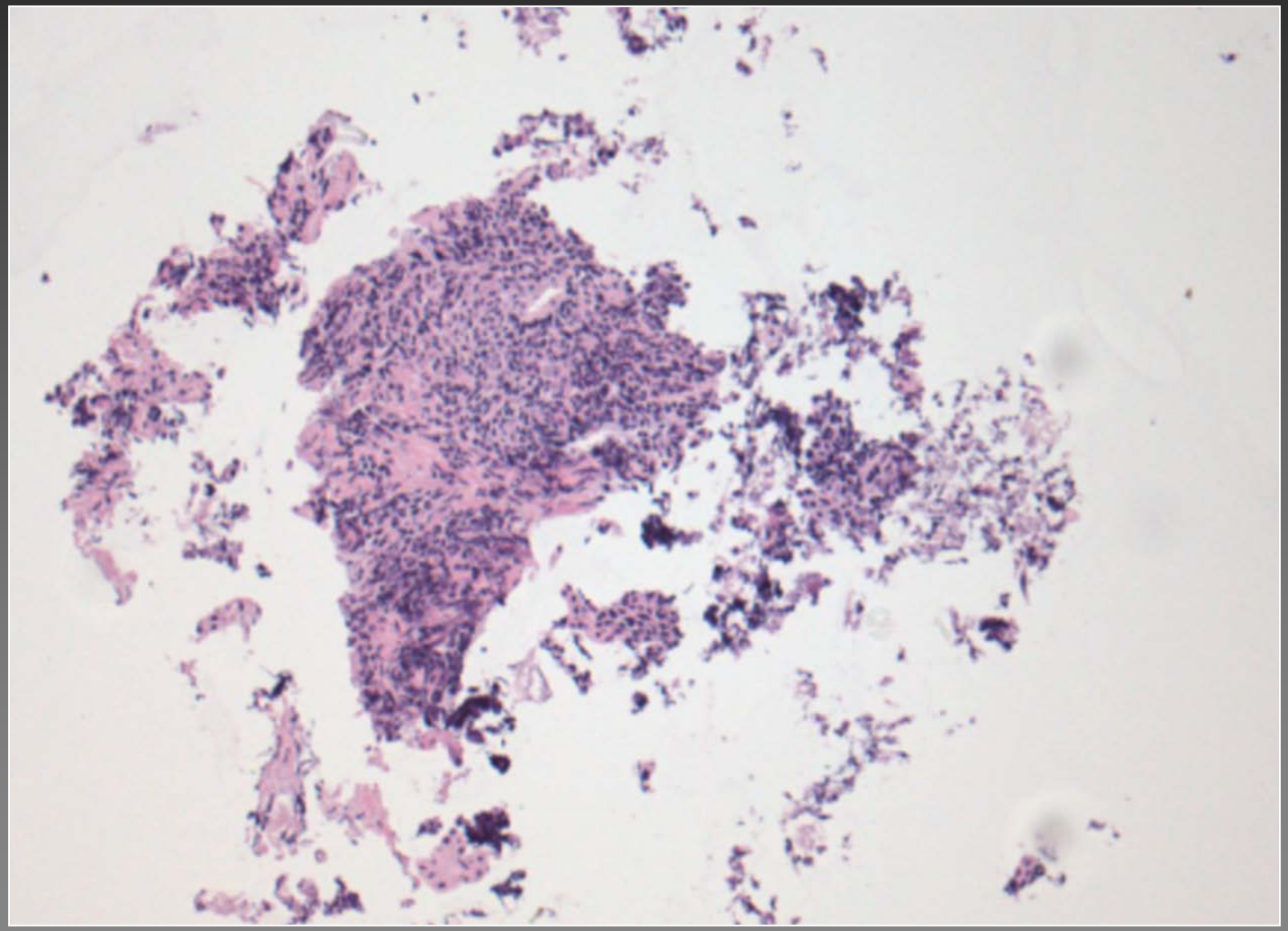


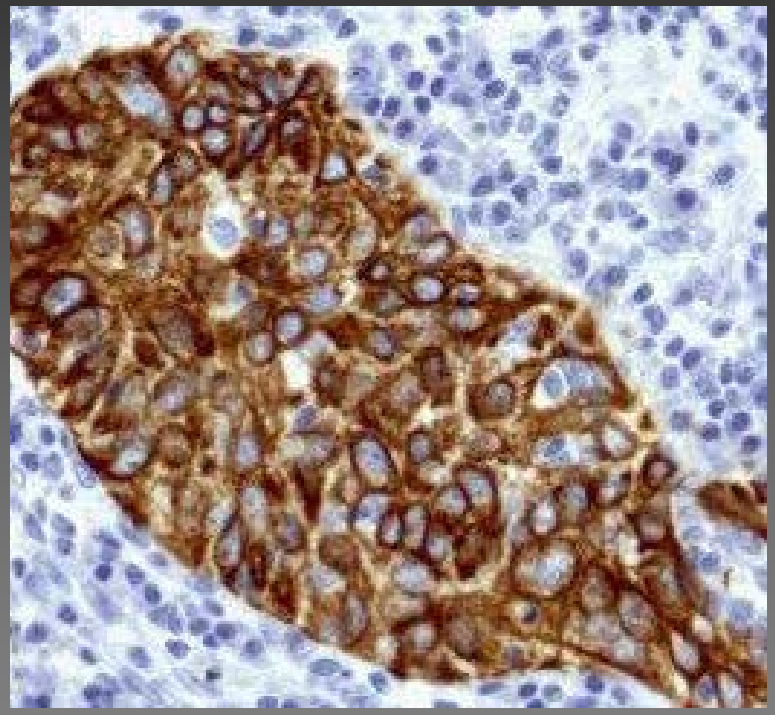
Case #1: FNA of Neck Mass

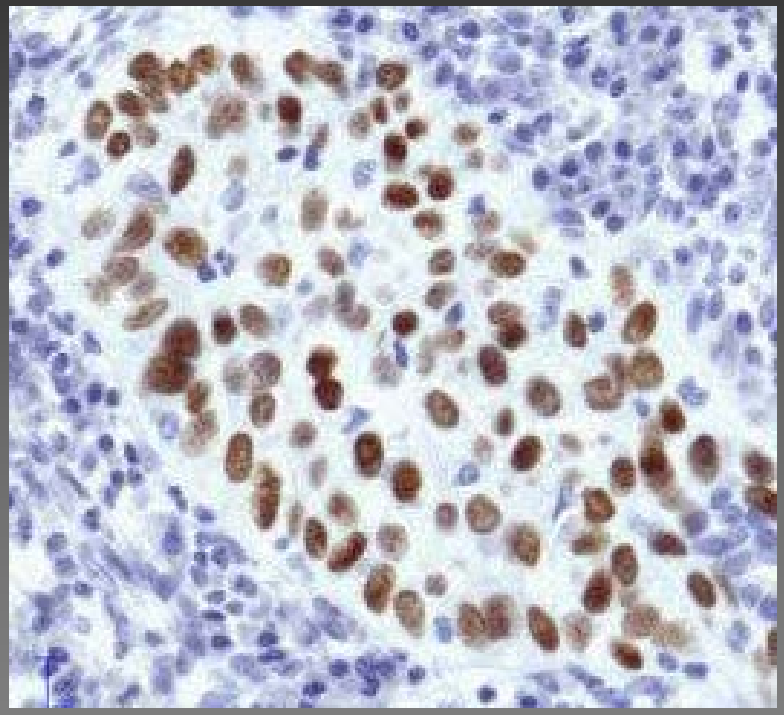


Case #1: FNA of Neck Mass – cell block

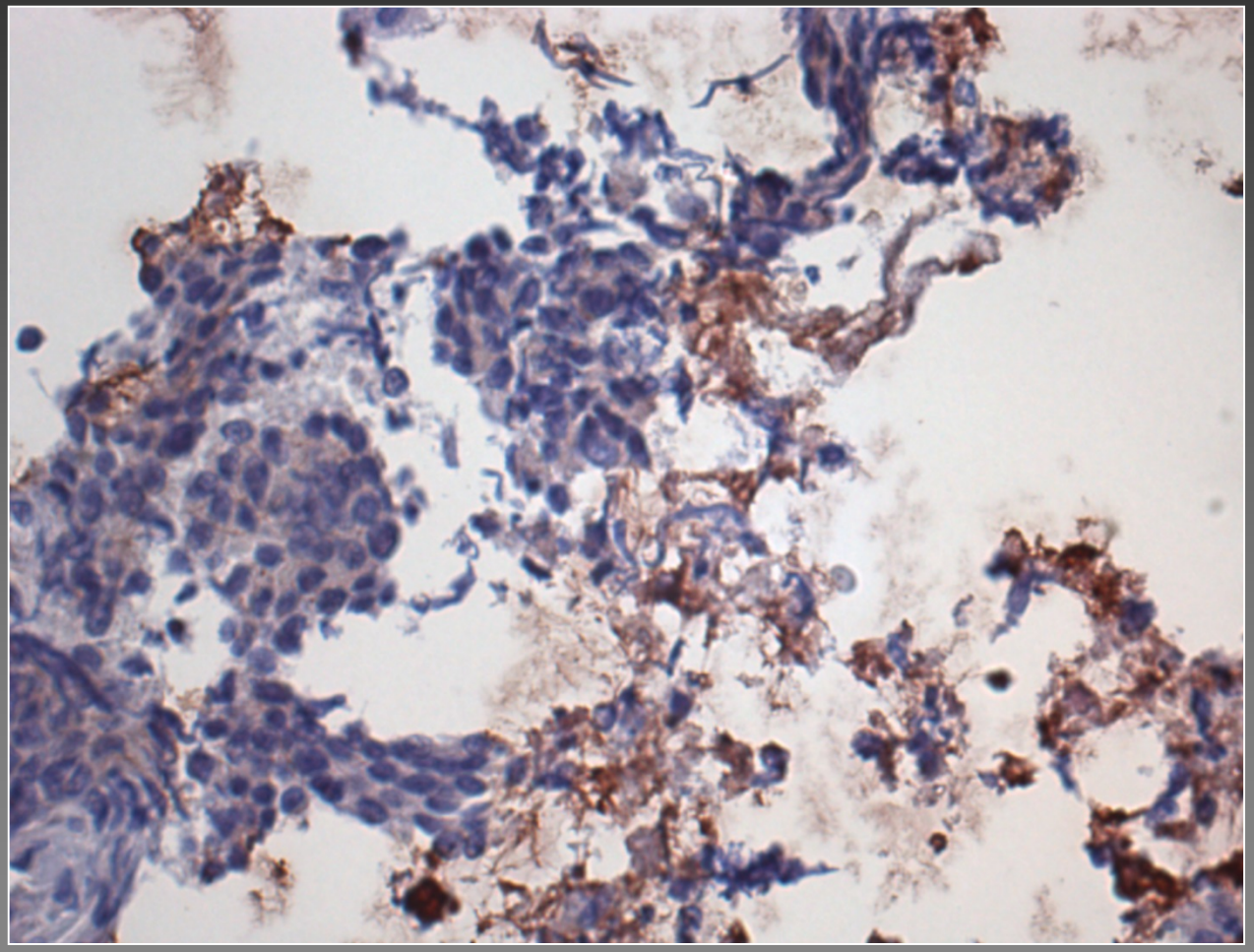


Case #1: CK 5 and P63 on Cell Block

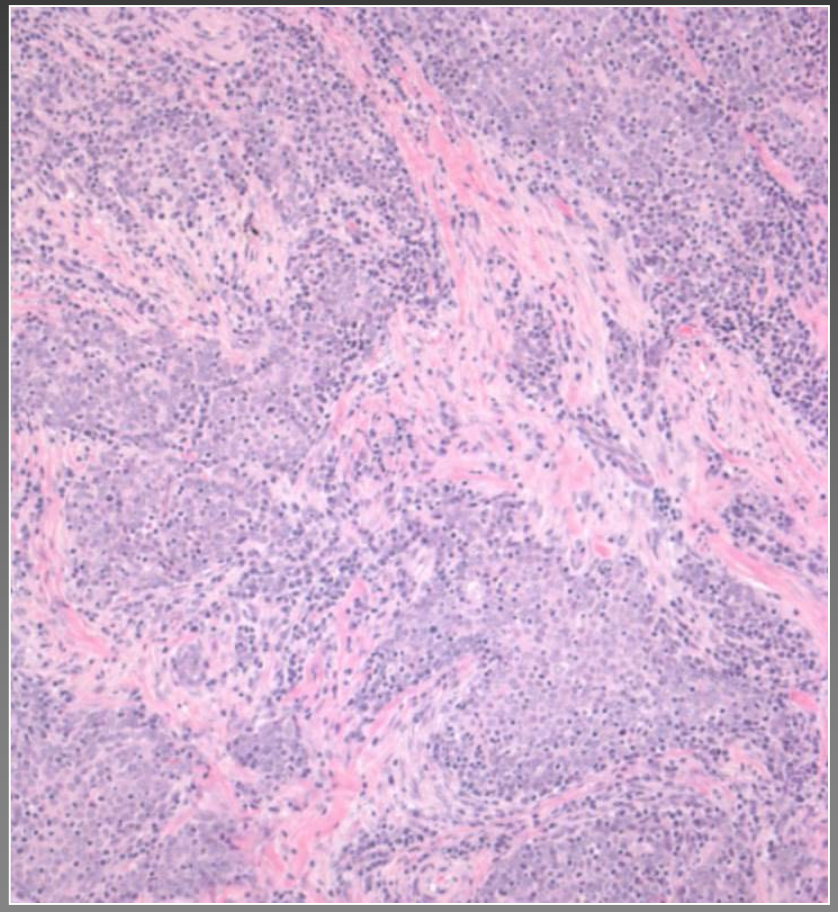


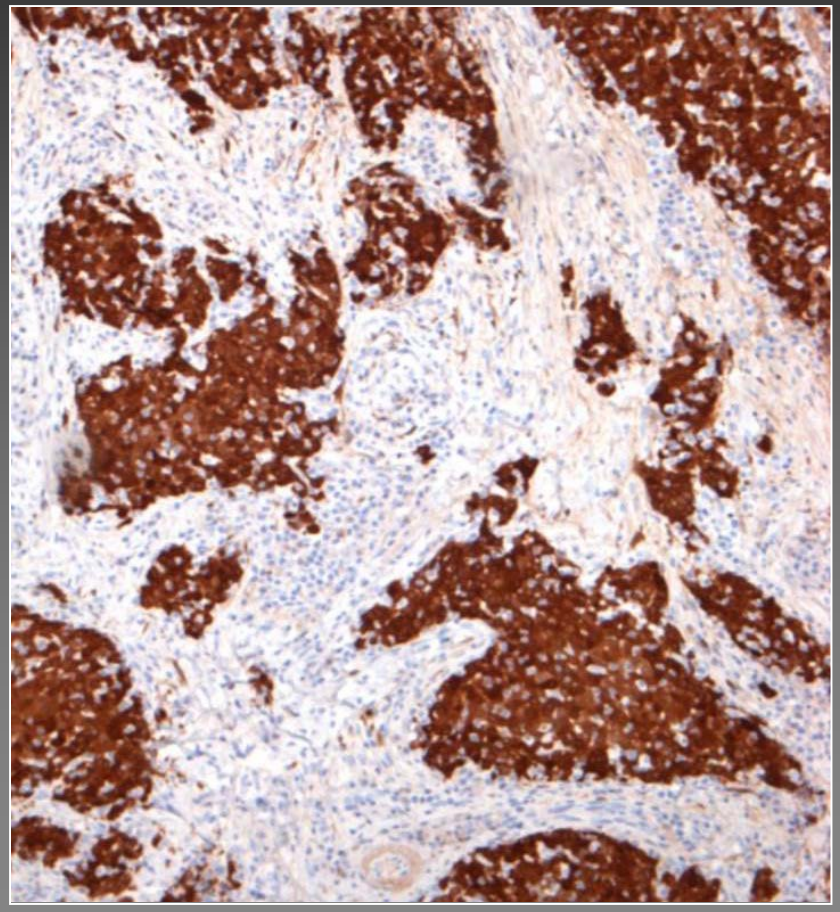


Case #1: FNA of Neck Mass –p16



Case #1 – Surgical Specimen -H/E and p16 of Neck Mass

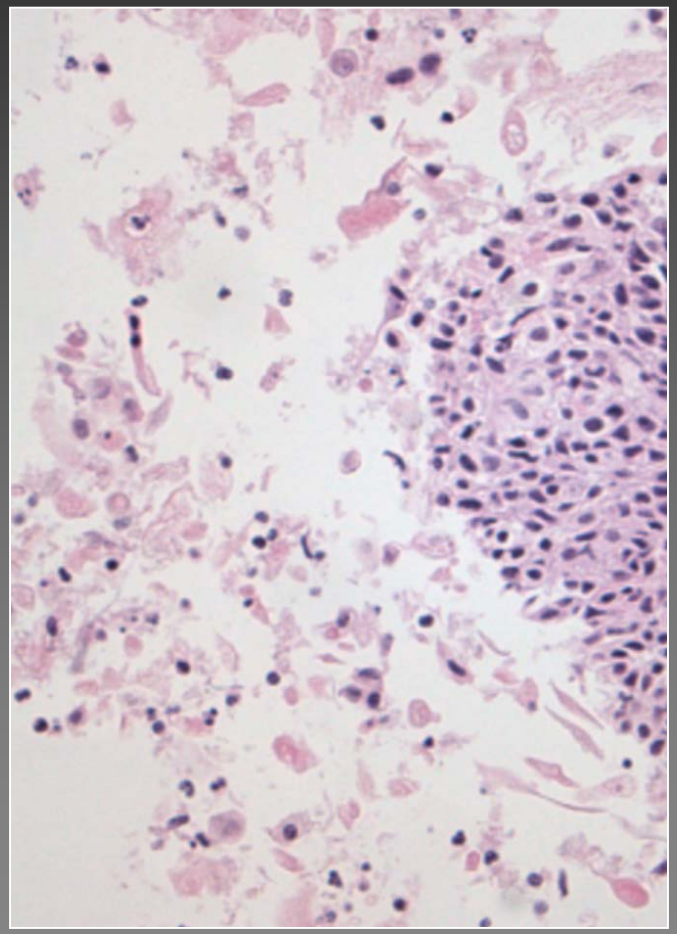


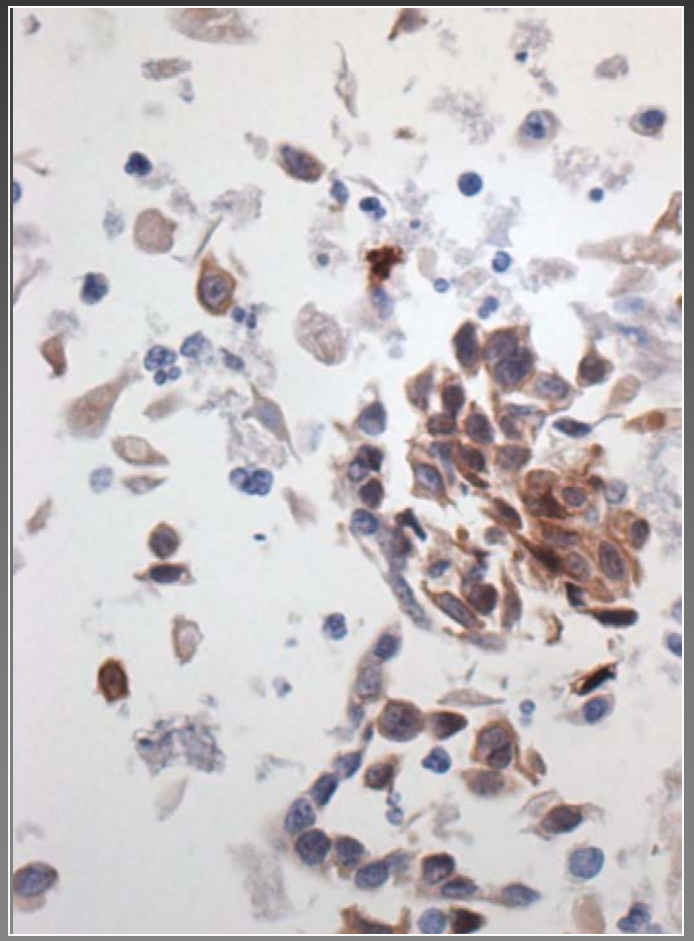



WHICH ONE OF YOU SHOULD I BELIEVE???

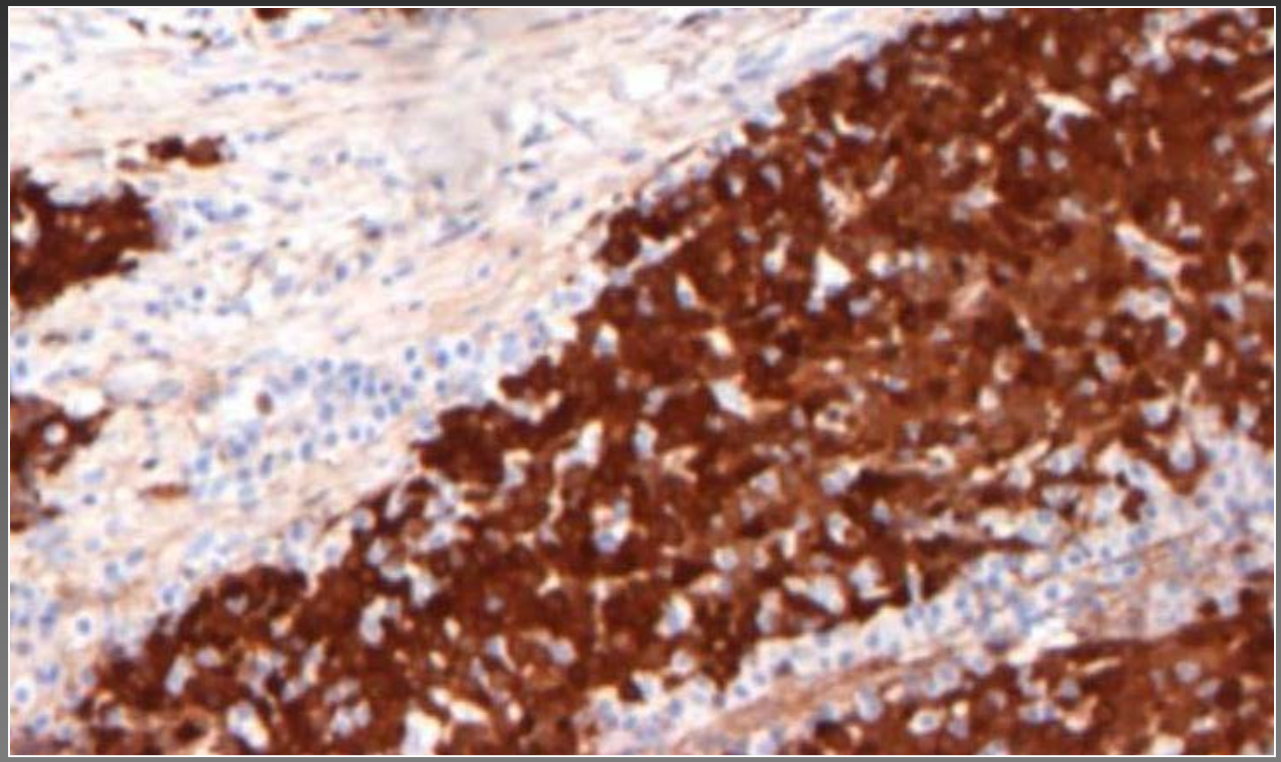

WE MUST GO TO EARTH
RIGHT NOW !!!
There is a p16 discrepancy

Case #2: FNA of Neck Mass – cell block H/E and p16





Case #2: p16 on Surgical Specimen



How do we explain these ‘false negatives’ and what should we do?

- Preanalytic, analytic and postanalytic conditions
- Validation and optimization must be carried out in our laboratories

Procedures for the IHC detection of p16 in FNA material which is alcohol fixed are currently undergoing validation and optimization in this laboratory. These results, particularly if negative must be interpreted with caution. IHC for p16 has been validated on formalin fixed tissue.

Correlation of p16 IHC in FNA Material with Corresponding Tissue Specimens in HPV-Related SCC of the Oropharynx

- The recommended threshold (70% positive staining) for surgical pathology specimens will yield a high rate of false-negative results if applied to cell blocks (Jalaly et al, Cancer Cytopathol 2015; 123: 723-31)

- Excellent correlation between p16 IHC of FNA cell block and surgical specimens using a cutoff of 15% (Jajlay et al, 2015) or 10% (Zu et al, 2016) positive staining of cells in cell block

HPV Testing in FNAs of Squamous Cell Carcinoma of Head and Neck

Liquid phase testing:

- Objective results
- Can be automated
- Several platforms have been validated for FNA of SCC of unknown primary:
  - Hybrid Capture II
  - Cervista TM HPV
  - Roche Cobas HPV test
  - APTIMA HPV assay

Screening and Prevention of HPV Associated Head and Neck SCC

- No recognized precursor lesion or intervention
- HPV vaccination - no known effects as of yet on the incidence of HNSCC

Summary

- HPV-related oropharyngeal squamous cell carcinoma (OPSCC) is a distinct disease that is associated with better prognosis and treatment response
- Reflex testing for HR-HPV in OPSCC and nodal metastatic SCC with unknown primary
- Liquid bases HPV testing is likely to be increasingly useful in aspiration cytology